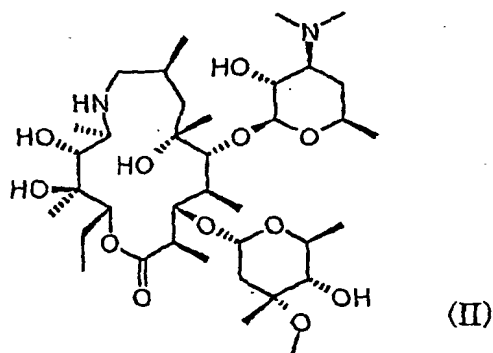
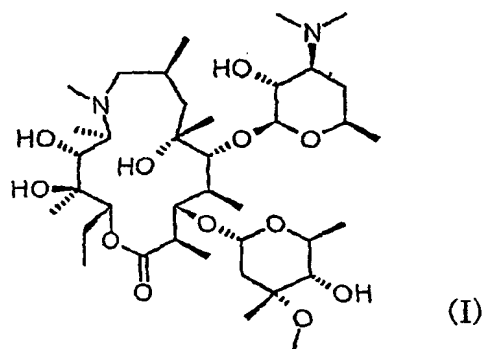
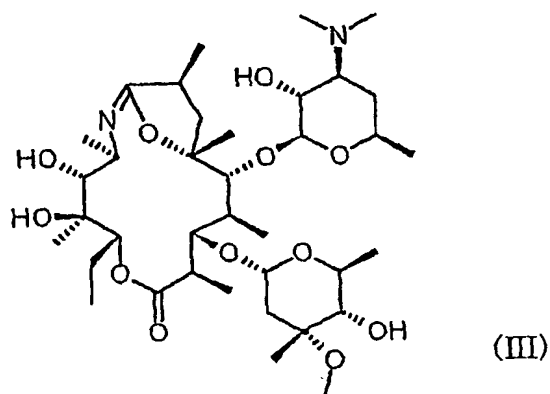


WHAT IS CLAIMED IS :

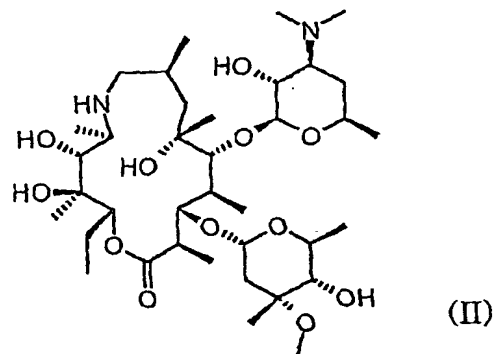
1. A method of preparing azithromycin of formula (I) comprising the steps of: (a) reducing 6,9-imino ether of formula (III) dissolved in methanol with 5 to 7 mole equivalents of  $\text{NaBH}_4$  at  $-20$  to  $-10^\circ\text{C}$ , treating the reaction mixture with an acidic aqueous acetone solution of citric acid, and adjusting the solution pH to 10.5 to 12.0 to obtain a crystalline hydrate of 9-deoxo-9a-aza-9a-homoerythromycin A of formula (II); and
- 10 (b) N-methylating the compound of formula (II) prepared in step (a) with an aqueous formaldehyde-formic acid mixture in an organic solvent:





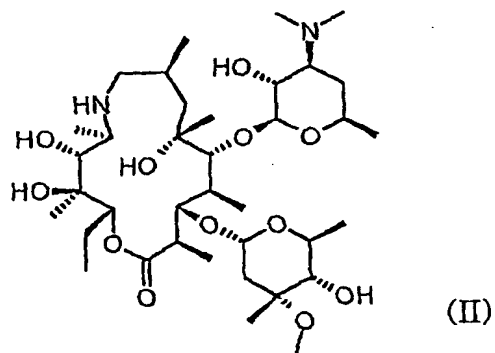
2. The method of claim 1, wherein citric acid is used in an amount ranging from 1 to 20 mole equivalents based on 1 mole of 6,9-imino ether of formula (III).
3. The method of claim 1, wherein the pH of the acidic solution is in the range of 2.0 to 3.0.
4. The method of claim 1, wherein the amount of acetone in the aqueous acetone solution is in the range of 1 to 5 ml per 1 g of the compound of formula (III), and the water to acetone volume ratio is in the range of 1 to 4.
5. The method of claim 1, wherein the organic solvent used in step (b) is selected from the group consisting of dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane, methanol, ethanol, isopropanol, acetone, ethylmethylketone, isobutylmethylketone, methyl acetate, ethyl acetate, isopropyl acetate and a mixture thereof.
6. The method of claim 1, wherein the amounts of formic acid and formaldehyde used are each independently in the range of 1 to 3 mole equivalents per 1 mole of the compound of formula (II).
7. A crystalline hydrate of 9-deoxy-9a-aza-9a-homoerythromycin A of formula (II) whose powder X-ray diffraction spectrum ( $I/I^\circ \geq 10$ ) shows peaks at  $2\theta$  values of  $7.700^\circ \pm 0.2$ ,  $8.080^\circ \pm 0.2$ ,  $10.080^\circ \pm 0.2$ ,  $11.440^\circ \pm 0.2$ ,  $12.200^\circ \pm 0.2$ ,  $13.840^\circ \pm 0.2$ ,  $14.100^\circ \pm 0.2$ ,  $14.520^\circ \pm 0.2$ ,  $14.820^\circ \pm 0.2$ ,

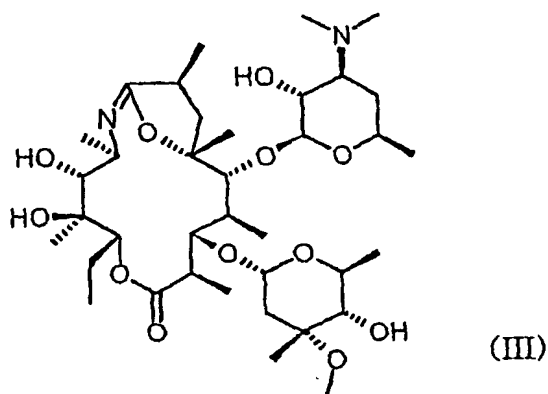
15.140° ± 0.2, 15.800° ± 0.2, 16.780° ± 0.2, 17.260° ± 0.2, 18.160° ± 0.2, 18.900° ± 0.2, 19.180° ± 0.2, 19.800° ± 0.2 and 21.040° ± 0.2:



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8. The crystalline hydrate of claim 7 which is a monohydrate.
9. A method of preparing the crystalline hydrate of claim 7 comprising the steps of: (i) reducing 6,9-imino ether of formula (III) dissolved in methanol with 5 to 7 mole equivalents of NaBH<sub>4</sub> at -20 to -10 °C, (ii) treating the reaction mixture with an acidic aqueous acetone solution of citric acid, and (iii) adjusting the solution pH to 10.5 to 12.0:
- 10





10. The method of claim 9 which further comprises the step of recrystallizing the crystalline hydrate from a mixture of water and an organic solvent selected from acetone, methanol and acetonitrile.

11. The method of claim 10, wherein the organic solvent is used in an amount ranging from 1 to 2 ml per 1 g of the crystalline hydrate, and the water to organic solvent volume ratio is in the range of 1 to 4.